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Differential Diagnosis of Congenital Heart Disease in the Newborn

STANLEY KIRKPATRICK, MD:* *In the newborn nursery it is frequently a problem to determine the presence or absence of congenital heart disease. We have endeavored to develop a simplified approach to alert nursery physicians or nurses to the possibility of underlying congenital heart disease and its differentiation from other causes of cyanosis, including pulmonary parenchymal disease. This problem will be illustrated by the case presentation.*

ADALINE CORRIN, MD.† The infant was a boy born to a 24-year-old gravida 2, para 1, aborta 1 mother. The pregnancy was complicated by a positive Venereal Disease Research Laboratories test (VDRL) in the first month of pregnancy; treatment was carried out with penicillin. The baby had Apgar scores of 7 and 8 at one and five minutes. He was meconium stained at birth. The weight was 5 pounds 3 oz and the baby was judged to have been born at approximately 35 weeks gestation. Immediately after birth the baby was noted to be tachypneic. Initial heelstick blood gas values were: pH 7.36, carbon dioxide pressure (Pco_2) 46 and oxygen pressure (Po_2), 37 mm of mercury. He was treated with 40 percent oxygen by hood and repeat gas values were pH 7.36, Pco_2 40 and Po_2 64 mm of mercury. The findings on the initial roentgenogram of the chest were not clearcut. They were interpreted as being consistent with either increased pulmonary venous markings or meconium aspiration. At four days of age he began to have more retractions and grunting, and his color was more dusky. He was transferred to University Hospital, San Diego.

On arrival the baby was in moderate respiratory distress. The respiratory rate was 80 to 100. There were nasal flaring, grunting and intercostal retractions. Rales were heard over both lung fields. The heart rate was 140 to 150 beats per minute. The second sound was closely split and the intensity of the pulmonic second sound (P_2) was accentuated. There was a continuous murmur best heard in the second and third left intercostal spaces and in the infraclavicular area on the left. Pulses were normal. The blood pressure was 61 mm of mercury in the left arm, 72 left leg and 65 right leg. The liver was palpated 2 to 3 cm below the costal margin.

The leukocyte count was 7,100 per cu mm and the hematocrit 44 percent. Cultures for bacteria were negative. The IgM was 15. Titer for cytomegalovirus (CVM) was 1:64, varicella, less than 1:8 and herpes simplex 1:32. The VDRL was nonreactive. X-ray studies of the chest were confusing and will be discussed by Doctor Higgins. An electrocardiogram showed a right axis deviation and peaked P waves, consistent with cor pulmonale. Treatment was continued with penicillin and gentamicin. Tachypnea and intermittent retractions, flaring and grunting continued. A cardiac catheterization showed pulmonary venous desaturation. Right ventricular and main pulmonary artery pressures were elevated to systemic levels. There was a small patent ductus arteriosus and a patent foramen ovale. Following catherization, the murmur decreased to a pronounced degree, and on an x-ray film of the chest more infiltrate was seen on the right than on the left. The infant

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TABLE 1.—*The Five Cardinal Findings in Infants With Congenital Heart Disease*

- Heart murmur
- Congestive heart failure
- Cyanosis
- Abnormal heart rate
- Tachypnea

did well in room air, and gas values were Po_2 42 and Pco_2 46 mm of mercury.

WILLIAM NYHAN, MD, PH D:* *Thank you, Dr. Corrin. You indicated that the x-ray studies of the chest were somewhat confusing. Let us turn now to Doctor Higgins for a discussion of these roentgenograms.*

CHARLES HIGGINS, MD:† The initial x-ray films of the chest showed a large increase in the interstitial markings in the right lung. All of the vessels were indistinct, particularly on the right side, indicating a substantial interstitial and alveolar filling process. There was more infiltrate in the right lung than in the left, a fact that is somewhat atypical for congestive heart failure, but certainly not something that is never seen. There was a large heart. The cardiothoracic ratio was over 60 percent. There was also a small right pleural effusion. The pulmonary findings suggested a diagnosis of aspiration pneumonia, but an enlarged heart is usually not seen in aspiration pneumonia, even in severe instances. In a large series of patients with meconium aspirations the cardiothoracic ratio was below 60 percent in almost all patients.

A radiograph obtained two days later showed persistent infiltrate in the right lung, but almost complete clearing on the left side. The heart size was still somewhat enlarged. Of course, clearing of infiltrate on the left side, along with persistent infiltrate on the right side was more in keeping with an aspiration pneumonia. Most cases of aspiration pneumonia clear within three days. Many are clear within 24 hours on x-ray studies. A film obtained one day later showed the left lung almost normal and the right lung with some persistent infiltrate. The heart size had decreased slightly. The most recent film obtained showed some persistent infiltrate in the right lung, a normal-sized heart and a normal pulmonary parenchymal pattern on the left.

DR. NYHAN: *Thank you, Dr. Higgins. Let us now turn to Dr. Kirkpatrick for a discussion of this problem.*

DR. KIRKPATRICK: The identification of those infants who are at increased risk for congenital heart disease is important so that they may be selected for a more careful cardiovascular examination.[1] In the general population the incidence of congenital heart disease is approximately eight per 1,000 live births and does not vary with race. Infants born to diabetic mothers have an increased risk of congenital heart disease.[2] Also at increased risk are twin infants, children with chromosomal abnormalities and babies born to mothers who have congenital heart disease. In these specific instances an infant requires special attention to the possibility of congenital heart disease.

There are five cardinal findings (Table 1) that suggest the presence of significant heart defects: (1) heart murmur, (2) congestive heart failure, (3) cyanosis, (4) abnormal heart rates and (5) tachypnea.

Heart Murmur

Heart murmurs (Table 2) are not easily heard in the noisy nursery, particularly when the infant is being monitored with an auditory signal and receiving assisted ventilation. Quiet surroundings are needed in order to auscultate adequately. If the child cannot be taken to a quiet place, then it is important to make the surrounding area as noise-free as possible. A murmur, heard at the newborn examination shortly after birth, when pulmonary vascular resistance is still high and pulmonary pressure is essentially equal to systemic, indicates that the underlying lesion is most likely obstructive or an insufficient valve. The diagnoses to be considered are aortic stenosis,

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TABLE 2.—*Relationship of the Type of Cardiac Defects and the Age at Which the Murmur Is First Noted*

Age	*Defect*
Birth	Obstructive lesions with pressure gradient: aortic stenosis, pulmonary stenosis, coarctation, regurgitant A-V or semilunar valves MI, TI, AI, PI.
Discharge from nursery	All of the previous lesions. Left to right shunts as pulmonary vascular resistance drops: ventricular septal defect, patent ductus arteriosus.
Routine 6-week visit	Left to right shunts more pronounced with further drop in pulmonary vascular resistance.
4 to 6 years	Atrial septal defect.

pulmonic stenosis, and mitral or tricuspid regurgitation. Coarctation of the aorta is more likely to be found a little later when the patent ductus arteriosus is fully closed. Murmurs in the immediate newborn period rarely indicate the presence of a left to right shunt since the pressures and resistances are very nearly equal in the right and left heart chambers.

As the pulmonary vascular resistance and pressure begin to fall, murmurs resulting from left to right shunts appear. Therefore, if no murmur was noted at the initial newborn examination but one is found at 3 days of age, the possibility of a ventricular septal defect or a pathologic patent ductus arteriosus should be considered. It is possible to hear a nonpathologic continuous murmur in infants during the first 24 hours which then disappears on the following day as the ductus closes physiologically.

At the six week evaluation, the pulmonary vascular resistance has dropped sufficiently so that a left to right shunt through a ventricular septal defect will be apparent. In contrast, the murmur of an atrial septal defect is usually first noted at 4 to 6 years of age. It is more common in these children for there to be a gradual increase in their left to right shunt over a period of years because of the minimal gradient across the atrial septum and the compliance characteristics of the two ventricles.

Congestive Heart Failure

The signs and symptoms of congestive heart failure in the newborn period are distinctly different from those seen in adults.[3] Peripheral edema, a very common finding in adults with congestive heart failure, is a late sign in infants. The initial signs of failure in infants are usually respiratory distress, tachycardia, inappropriate weight gain and an enlarged liver. The nurses will frequently indicate that the infant is a poor feeder with an above average respiratory and heart rate. The color may be poor and the urinary output decreased. Any such infant should be examined carefully for the possibility of congenital heart disease. Infants with congestive heart failure commonly have a very consistent heart rate of 160 to 180 because of a predominant sympathetic discharge which also helps to explain the diaphoresis often seen in these children.

The liver in the newborn infant is virtually always palpable and may be as much as 3 cm below the right costal margin normally. It is important to distinguish between a liver that is displaced inferiorly and a liver that is truly enlarged because of congestion from heart failure. In the latter instance, the liver may be boggy or firm and have a blunted edge which is frequently directed posteriorly. Children with respiratory distress may have flattened diaphragms and livers which are displaced inferiorly but their consistencies and edges are entirely within normal limits.

Gallop sounds are often heard in small infants who have congestive failure if the examiner is patient and listens in a quiet atmosphere. Rales in the lung fields are often present, and they appear in both right-sided and left-sided heart failure. Pulmonary edema as a sign of primary left heart failure and liver engorgement as a sign of primary right heart failure are less reliable in infants than in adults. It is most common for there to be concomitant evidence of both right and left heart failure in infants.

Since the newborn myocardium is functioning at the peak of its ventricular function curve, it does not tolerate volume overload well. Consequently, common causes of congestive heart failure in the newborn include diagnoses such as arterial venous fistulae, maternal-fetal or twin-twin transfusions, and rapid volume expansion from an indwelling catheter, all of which represent volume overload. Various forms of congenital heart disease do not usually cause failure at or shortly after birth but there are a few exceptions, such as tricuspid regurgitation, absent pulmonary valve, supraventricular tachycardia and hypoplastic left heart syndrome with early closure of the ductus arteriosus.

Neonatal asphyxia with resultant acidemia, hypoglycemia and hypocalcemia can precipitate myocardial failure. An uncommon cause of failure is embolization of the coronary artery which results in myocardial infarction during or shortly after delivery.[4] Myocardial infarctions in infants present with an electrocardiographic pattern which is quite diagnostic. Anomalous left coronary artery may also cause infarction in infants; however, symptomatology usually occurs after a week of life when pulmonary arterial pressure and resistance have dropped to levels which provide inadequate coronary profusion.

Cyanosis

The third major finding in infants with congenital heart disease is cyanosis (Figure 1). There are three types of cyanosis: central, peripheral

and differential. Central cyanosis is characterized by arterial desaturation within the aorta. Peripheral cyanosis, on the other hand, simply indicates stasis of blood flow in the periphery with greater than 3 grams per 100 ml of desaturated hemoglobin. It does not mean that there is desaturation within the central aorta. Most of these patients are cool peripherally, and warming usually restores normal color.[5] Differential cyanosis virtually always indicates congenital heart disease. Coarctation is usually part of the complex. If the upper part of the body is pink and the lower body blue, this indicates a coarctation of the aorta with oxygenated blood supplying the upper body and desaturated blood supplying the lower body via retrograde flow through the ductus. A patient with transposition, coarctation and retrograde flow through a patent ductus arteriosus shows the reverse situation with the lower portion of the body pink and the upper portion blue. Simultaneous determinations of oxygen saturation in the right brachial artery and the femoral artery are helpful in confirming the presence of differential cyanosis.

Central cyanosis results from either an abnormal hemoglobin (methemoglobinemia) or from a failure of hemoglobin to come in contact with oxygen. The diagnosis of methemoglobinemia as a cause of central cyanosis is usually easily made, providing one thinks of the possibility. Normally, when heparinized venous blood is exposed to room air it becomes pink. In persons who have methemoglobinemia, the blood remains dark. A suspicion of methemoglobinemia is confirmed by obtaining a saturation and a Po_2 in the blood gas laboratory. This analysis will show a normal partial pressure of oxygen and a low oxygen saturation. The definitive diagnosis can be made by electrophoresis.

For the purposes of discussion, let us assume that the above mentioned forms of cyanosis have been ruled out, and we are left with a patient who has a low oxygen saturation in both the upper and lower extremities while breathing room air. The next step is to carry out ventilation in the child using 100 percent oxygen and obtain arterial blood gas values again. I prefer that ventilation in the neonate be done by mechanical means, either via endotracheal tube or mask, so that the possibility of inadequate ventilatory effort is excluded. After equilibration, repeat blood gas determinations are obtained. If the Po_2 and oxygen saturation are essentially unchanged, this indicates the presence of blood bypassing the lungs, as occurs in infants with congenital heart disease and a right to left shunt. If, on the other hand,

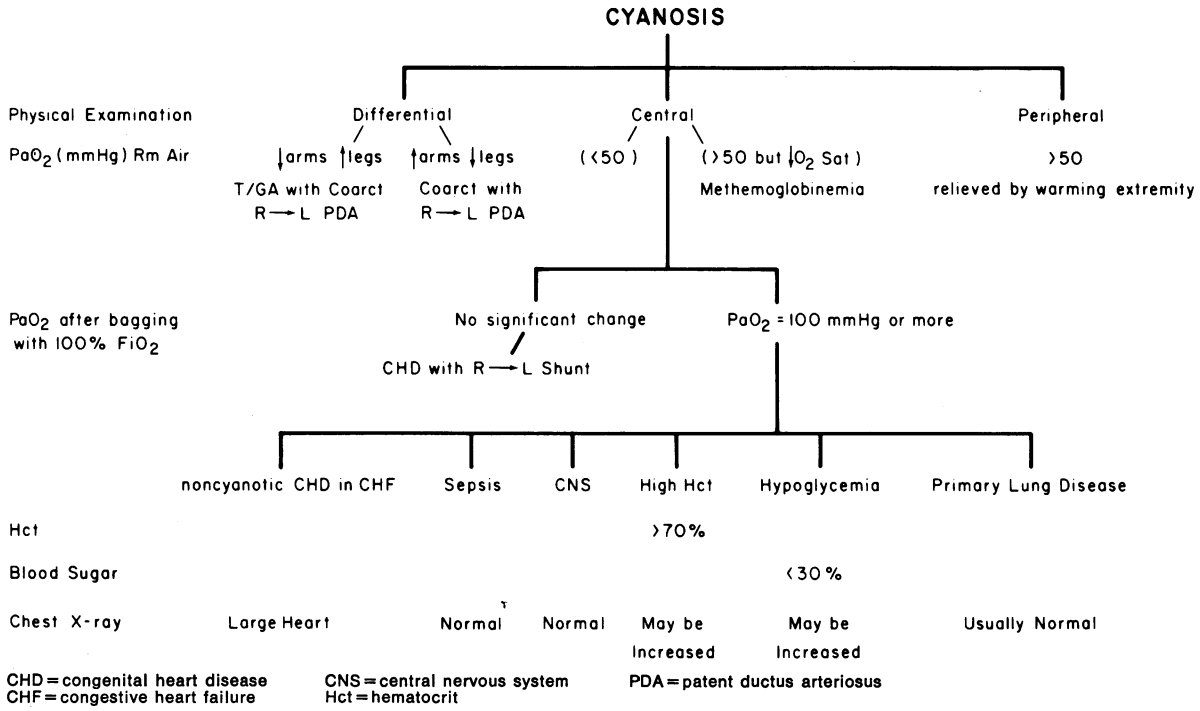
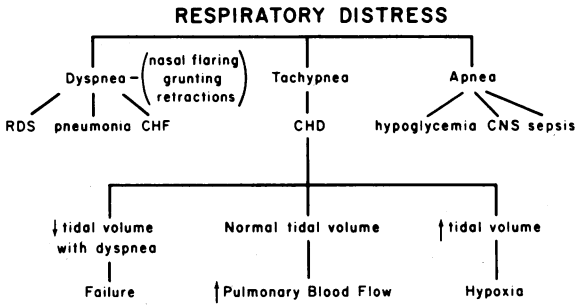


Figure 1.—Flow chart for the evaluation of cyanotic patients. Tests to be done are listed at the left. A patient's response to each of these tests leads along the line to the proper diagnosis.



CHD = congenital heart disease CNS = central nervous system
CHF = congestive heart failure RDS = respiratory distress syndrome

Figure 2.—Differential diagnosis of respiratory disease. Analysis of aspects of respiratory distress which are useful in the diagnosis of specific disease entities.

a significant rise in oxygen saturation is seen such that the Po_2 reaches 100 mm of mercury or greater, the infant most likely has primary pulmonary disease. However, some infants who have acyanotic congenital heart disease with congestive heart failure may show significant improvement with assisted ventilation. These infants can usually be differentiated from those with pulmonary disease by the presence of cardiomegaly in roentgenograms.

Heart Rate

The fourth cardinal finding that heralds the presence of congenital heart disease is an abnormal heart rate which may either be excessively fast or unusually slow. When the heart rate is 240 to 300 (paroxysmal supraventricular tachycardia), congestive heart failure will develop because of inadequate time for diastolic filling. If the heart rate is 50 or below the infant will have congestive heart failure because of inadequate cardiac output. Although stroke volume increases remarkably, cardiac output is still insufficient to meet the child's demands because the heart rate is so slow. Our current mode of therapy for paroxysmal atrial tachycardia is electroconversion using 1 to 2 watt seconds per kg of body weight.

Following conversion, digitalis is given and administration of the usual dose of digoxin (Lanoxin®), 12 to 15 μg per kg of body weight in divided doses every 12 hours, is maintained. Treatment for the infant with complete congenital heart block and a heart rate of 50 or less is permanent pacing. If, on the other hand, the heart rate is 60 or greater, it is likely that stroke volume will increase sufficiently to meet demands for growth. The prognosis for patients with paroxysmal atrial tachycardia or complete heart block is much better if there is no associated congenital heart disease.

TABLE 3.—*Diagnostic Aids in Differential Diagnosis of Congenital Heart Disease*

History and physical examination
Hematocrit, electrolytes, calcium, glucose studies
Blood gas determinations on room air and bagging with 100 percent forced inspiratory oxygen
X-ray film of the chest
Electrocardiogram
Echocardiogram
Cardiac catheterization

Tachypnea

The fifth finding that alerts to the possibility of congenital heart disease is an abnormal respiratory rate (Figure 2).[6] Isolated tachypnea is the most common pattern. If the child is in congestive heart failure, dyspnea will be among the clinical features. On the other hand, if dyspnea is the primary finding with flaring of the alae nasi, retractions and grunting, primary pulmonary disease is the more likely cause.

Once one of the five cardinal findings of congenital heart disease has been recognized, our workup consists primarily of the studies listed in Table 3. Careful assessment of the peripheral pulses is a simple procedure worth emphasis. It must be a part of all cardiac evaluations. The diagnosis of coarctation of the aorta is made if femoral pulses are absent. If the pulses are bounding in a premature infant a diagnosis of patent ductus arteriosus may be strongly suspected. The second physical finding that should be emphasized is the position of the liver. A horizontal liver or a liver on the same side as the cardiac apex should raise the question of visceral heterotaxy and the associated asplenia-polysplenia syndrome.

Helpful Radiographic Findings

There are five aspects of roentgenograms that have been significantly helpful in the diagnosis of congenital heart disease. The first is the presence of a right-sided aortic arch. This finding, in association with decreased pulmonary blood flow, is indicative of tetralogy of Fallot. A right aortic arch in the presence of increased pulmonary blood flow suggests a truncus arteriosus or transposition of the great arteries. Differential pulmonary blood flow, the second sign, can be seen in persons with tetralogy of Fallot, hemitruncus and absence of

one of the pulmonary arteries. The third sign is a characteristic shape of the heart, which is often helpful when present. The egg-on-egg appearance with a narrow base is typical of transposition of the great arteries, and a boot-shaped heart with concavity of the pulmonary outflow is consistent with tetralogy of Fallot. An abnormal position of the cardiac apex, the fourth sign, is seen in the scimitar syndrome[7] or the asplenia-polysplenia syndrome. Last, pulmonary vascular markings indicate the amount of pulmonary blood flow. In a patient with a large main pulmonary artery, increased pulmonary arterial markings would indicate an atrial septal defect, while normal pulmonary arterial markings are consistent with pulmonary valvular stenosis.

Helpful Findings on Electrocardiograms

Newborn infants normally have a right ventricular pattern reflecting intrauterine hemodynamics in which the right and left ventricular pressures are the same. At birth, an electrocardiogram in an infant usually shows balanced right and left precordial forces and apparent right ventricular hypertrophy, compared with the adult pattern. Abnormal right ventricular hypertrophy is usually seen in forms of congenital heart disease, such as transposition of the great arteries, tetralogy of Fallot, pulmonary atresia with ventricular septal defect, pulmonary stenosis, double outlet right ventricle, arteriovenous fistula and total anomalous pulmonary venous return. If one sees, on the other hand, a left ventricular predominance, a diagnosis of tricuspid atresia should be suspected. Patients who have a counterclockwise superiorly oriented frontal plane loop often have an endocardial cushion defect. An infarction pattern in the newborn is not common; it is diagnostic of coronary embolism.[4] An anomalous left coronary artery arising from the pulmonary artery does not cause an infarct pattern until several days of life when pulmonary pressure and resistance have dropped sufficiently to provide inadequate coronary perfusion.

Echocardiography is a relatively new modality which has become invaluable in cardiac evaluation. Catheterization and angiography continue to be the most reliable tools in the diagnosis of congenital heart disease, and definition of intracardiac anatomy.

In summary, there are five major findings in the newborn period that should alert a nurse or physician to the possibility of congenital heart disease. These are heart murmur, congestive heart failure, cyanosis, abnormal heart rate and tachypnea. It is important to obtain simultaneous upper and lower compartment blood gas determinations while the patient is breathing room air and 100 percent oxygen. If there is a significant increase in the Po_2 while the patient is breathing 100 percent oxygen, the infant most likely has primary pulmonary disease. On the other hand, if there is little or no increase in oxygen saturation while the patient is breathing 100 percent oxygen, the presence of congenital heart disease must be ruled out.

DR. NYHAN: *In the case presented did you feel that the baby had congenital heart disease?*

DR. KIRKPATRICK: I did not feel that there was underlying congenital heart disease in this baby. The x-ray chest film showed evidence of increased markings, more on the left. On physical examination there was a soft ejection murmur with normal splitting of the second heart sound and no flow murmur. I believe the findings represented an increase in arterial blood flow to the left lung because it was the least involved with primary pulmonary disease.

Clinically our major concern was to rule out the presence of pulmonary venous obstruction. With the normal chamber sizes noted on echocardiograms, we felt we had ruled out a significant left to right shunt. During the catheterization I placed the catheter into the pulmonary veins without difficulty and found pulmonary venous pressure to be normal. The major decrease in pulmonary venous saturation was noted in the area of the lung which had the most evidence for parenchymal involvement. We felt certain that the patient did not have congenital heart disease and that the desaturation was on the basis of primary parenchymal disease.

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